REMARKS

Claims 2-6 are cancelled, and claims 12-16 are cancelled as drawn to non-elected subject matter. Claims 1 and 7 have been amended. Claims 17-19 have been added. The new and amended claims are supported throughout the application as filed, for example page 4, lines 18-20, and page 18, lines 26-29. No new matter has been added. Upon entry of this amendment, claims 1, 7-11, and 17-19 will be pending. Please consider the following remarks.

Drawings

A transmittal of formal drawings is submitted herewith.

35 USC § 122, second paragraph

Claims 1-11 have been rejected as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In one part of the rejection, the Examiner objects to the term "level." The Examiner asserts that it is unclear whether the applicant intends to refer to protein or nucleic acid expression "levels." Claims 2-6 are canceled. This rejection is respectfully traversed with regard to the pending claims. Claim 1 recites that syndecan-4 expression, level, or activity is decreased. This result is achieved through the administration of a syndecan-4 nucleic acid molecule that can bind to cellular syndecan-4 mRNA and inhibit expression of the protein, the administration of a syndecan-4 nucleic acid molecule that can bind to the coding strand of a double stranded cDNA molecule, or an antibody that specifically binds to the syndecan-4 protein. The mechanisms of these specific agents are well known in the art. Accordingly, one of skill in the art, would understand "level" to mean either the level of mRNA or protein, depending on which agent is administered. For example, where a recited syndecan-4 nucleic acid molecule is administered, one of skill in the art would understand that the level of syndecan-4 mRNA and/or protein would be decreased. Where a syndecan-4 antibody is administered, one of skill in the art would understand that the level of syndecan-4 protein activity would be decreased. Thus,

Applicant asserts that the term "level" is sufficiently clear to a skilled artisan and respectfully request that the rejection be withdrawn.

In another part of this rejection, the term "inhibitory form" in claims 5 and 6 is objected to. The recitation of the term "fragment" in claim 6 is also objected to. Claims 5 and 6 have been cancelled, rendering these rejections moot.

35 USC § 122, first paragraph

Claims 1-11 have been rejected as not being enabled. The Examiner asserts that while being enabling for methods of inhibiting angiogenesis through the generation of a transgenic syndecan-4 null animal, the claims are not reasonably enabled for a method of inhibiting angiogenesis through the administration of agents to a patient. This rejection has been met by amending claim 1 to recite specific, readily available agents that reduce syndecan-4. The present claims recite nucleic acid agents that either can bind to cellular syndecan-4 mRNA or are complementary to the coding strand of a double stranded cDNA molecule (i.e., antisense agents) and antibodies that specifically bind to a syndecan-4 protein. Support for antisense agents can be found on pages 18-21 of the specification and support for antibodies can be found on pages 22-25 of the specification. Claims 2-6 have been canceled. Thus, the claims have been substantially narrowed and no longer cover any and all possible agents. As presently amended, the claims are enabled.

The claims are enabled if one of ordinary skill in the art can make and use the claimed invention without undue experimentation. Applicant's example of a transgenic syndecan-4 null animal provides proof *in vivo* that reducing syndecan-4 inhibits angiogenesis. Accordingly, a skilled artisan could predict that the recited agents which decrease the expression, level, or activity of syndecan-4 would inhibit angiogenesis.

With regard to antibodies, Applicant notes that syndecan-4 antibodies were known at the time of filing. (See, e.g., Saoncella et al. Proc Natl Acad Sci U S A 1999 Mar 16;96(6):2805-10, copy enclosed). Further, the production of antibodies in general was well known in the art. Thus, it would not require undue experimentation to make and test antibodies that specifically inhibit syndecan-4, as required by the claims. This much has been made clear by the Federal Circuit. (See e.g., *In re Wands*, 858 F.2d 731. (Fed. Cir. 1988), where the court said that it

would not require undue experimentation to obtain antibodies needed to practice the claimed invention.). With regard to antisense molecules, as of the filing date of the application, it was routine in the art to identify antisense agents that would either bind to cellular syndecan-4 mRNA or the coding strand of a double stranded cDNA molecule (e.g., using gene walking technology). The use of antisense agents *in vivo* was also known at the time of filing. (See, e.g., Ma et al. (2000) *Biotechnology Annual Review* 5:155-196, copy enclosed, discussing several known antisense agents and their *in vivo* applications). Accordingly, it would not require undue experimentation to practice the presently claimed methods. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (MPEP § 2164.01). Further, a considerable amount of experimentation is permissible, if it is merely routine (MPEP §2164.06)

In summary, given the specific limitations recited in the claims, the high level of skill in the art, the detailed guidance provided by Applicants, the disclosure of an *in vivo* working example, and the routine nature of any experimentation that might be required to practice the claimed methods, the present claims are enabled. In view of the foregoing, Applicant respectfully requests that the rejection be withdrawn.